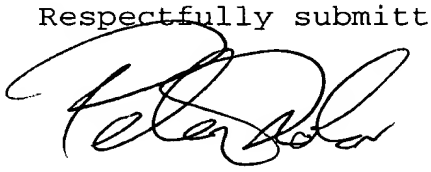
z is 1.

Conclusion

Applicants elected the species, Compound (V) and affirm their right to file one or more divisional applications with respect to any of the non-elected subject matter.

If a telephone interview would be of assistance in advancing prosecution of this application, Applicant's agent invites the Examiner to contact him at the number provided below.

Respectfully submitted,

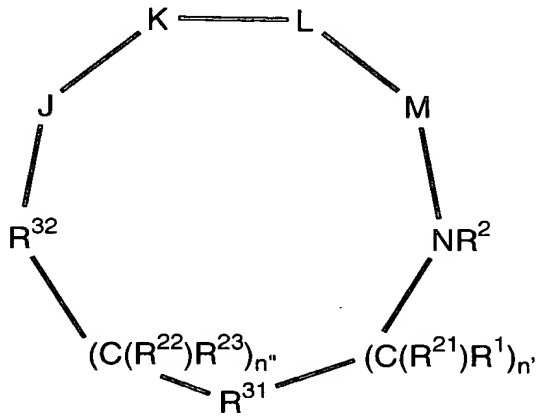


Dated: October 22, 2001

Peter L. Dolan, Ph.D.
Agent for Applicants
Registration No. 46,307
(302)992-4528

Appendix 1
Marked-Up Version of Rewritten Claims

6. (Amended) The method of Claim 4 wherein the localization step comprises the step of localizing a compound of the formula (I) at the thrombus wherein Q is of the formula (II),



(II)

or a pharmaceutically acceptable salt or prodrug form thereof wherein:

R^{31} is a C6-C14 saturated, partially saturated, or aromatic carbocyclic ring system substituted with 0-4 R^{10} or R^{10a};

R^{32} is selected from:
-C(=O)-;
-C(=S)-
-S(=O)2-;
-S(=O)-;
-P(=Z)(ZR^{13})-;

Z is S or O;

n" and n' are independently 0-2;

R^1 and R^{22} are independently selected from the following groups:

hydrogen,

C1-C8 alkyl substituted with 0-2 R^{11};

C2-C8 alkenyl substituted with 0-2 R^{11};

C2-C8 alkynyl substituted with 0-2 R^{11};

C3-C10 cycloalkyl substituted with 0-2 R^{11};

aryl substituted with 0-2 R^{12};

a 5-10-membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, said heterocyclic ring being substituted with 0-2 R^{12};

=O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{13}$, $-C(=O)R^{13}$, $-C(=O)N(R^{13})_2$, -CHO, $-CH_2OR^{13}$, $-OC(=O)R^{13}$, $-OC(=O)OR^{13a}$, $-OR^{13}$, $-OC(=O)N(R^{13})_2$, $-NR^{13}C(=O)R^{13}$, $-NR^{14}C(=O)OR^{13a}$, $-NR^{13}C(=O)N(R^{13})_2$, $-NR^{14}SO_2N(R^{13})_2$, $-NR^{14}SO_2R^{13a}$, $-SO_3H$, $-SO_2R^{13a}$, $-SR^{13}$, $-S(=O)R^{13a}$, $-SO_2N(R^{13})_2$, $-N(R^{13})_2$, $-NHC(=NH)NHR^{13}$, $-C(=NH)NHR^{13}$, $=NOR^{13}$, NO_2, $-C(=O)NHOR^{13}$, $-C(=O)NHNR^{13}R^{13a}$, $-OCH_2CO_2H$, 2-(1-morpholino)ethoxy;

R^1 and R^{21} can alternatively join to form a 3-7 membered carbocyclic ring substituted with 0-2 R^{12};

when n' is 2, R^1 or R^{21} can alternatively be taken together with R^1 or R^{21} on an adjacent carbon atom to form a direct bond, thereby to form a double or triple bond between said carbon atoms;

R^{22} and R^{23} can alternatively join to form a 3-7 membered carbocyclic ring substituted with 0-2 R^{12};

when n" is 2, R^{22} or R^{23} can alternatively be taken together with R^{22} or R^{23} on an adjacent carbon atom to form a direct bond, thereby to form a double or triple bond between the adjacent carbon atoms;

R^1 and R^2, where R^{21} is H, can alternatively join to form a 5-8 membered carbocyclic ring substituted with 0-2 R^{12};

R^{11} is selected from one or more of the following:

=O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{13}$, $-C(=O)R^{13}$, $-C(=O)N(R^{13})_2$, -CHO, $-CH_2OR^{13}$, $-OC(=O)R^{13}$, $-OC(=O)OR^{13a}$, $-OR^{13}$, $-OC(=O)N(R^{13})_2$, $-NR^{13}C(=O)R^{13}$, $-NR^{14}C(=O)OR^{13a}$, $-NR^{13}C(=O)N(R^{13})_2$, $-NR^{14}SO_2N(R^{13})_2$, $-NR^{14}SO_2R^{13a}$, $-SO_3H$, $-SO_2R^{13a}$, $-SR^{13}$, $-S(=O)R^{13a}$, $-SO_2N(R^{13})_2$, $-N(R^{13})_2$, $-NHC(=NH)NHR^{13}$, $-C(=NH)NHR^{13}$, $=NOR^{13}$, NO_2, $-C(=O)NHOR^{13}$, $-C(=O)NHNR^{13}R^{13a}$, $-OCH_2CO_2H$, 2-(1-morpholino)ethoxy,

C1-C5 alkyl, C2-C4 alkenyl, C3-C6 cycloalkyl, C3-C6 cycloalkylmethyl, C2-C6 alkoxyalkyl, C3-C6 cycloalkoxy, C1-C4 alkyl (alkyl being substituted with 1-5 groups selected independently from: $-NR^{13}R^{14}$, $-CF_3$, NO_2, $-SO_2R^{13a}$, or $-S(=O)R^{13a}$),

aryl substituted with 0-2 R^{12},

a 5-10-membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, said heterocyclic ring being substituted with 0-2 R^{12};

R^{12} is selected from one or more of the following:

phenyl, benzyl, phenethyl, phenoxy, benzyloxy, halogen, hydroxy, nitro, cyano, C1-C5 alkyl, C3-C6 cycloalkyl, C3-C6 cycloalkylmethyl, C7-C10 arylalkyl, C1-C5 alkoxy, $-CO_2R^{13}$, $-C(=O)NHOR^{13a}$, $-C(=O)NHN(R^{13})_2$, $=NOR^{13}$, $-B(R^{34})(R^{35})$, C3-C6 cycloalkoxy, $-OC(=O)R^{13}$, $-C(=O)R^{13}$, $-OC(=O)OR^{13a}$, $-OR^{13}$, -(C1-C4 alkyl)$-OR^{13}$, $-N(R^{13})_2$, $-OC(=O)N(R^{13})_2$, $-NR^{13}C(=O)R^{13}$, $-NR^{13}C(=O)OR^{13a}$, $-NR^{13}C(=O)N(R^{13})_2$, $-NR^{13}SO_2N(R^{13})_2$, $-NR^{13}SO_2R^{13a}$, $-SO_3H$, $-SO_2R^{13a}$, $-S(=O)R^{13a}$, $-SR^{13}$, $-SO_2N(R^{13})_2$, C2-C6 alkoxyalkyl, methylenedioxy, ethylenedioxy, C1-C4 haloalkyl, C1-C4 haloalkoxy, C1-C4 alkylcarbonyloxy, C1-C4 alkylcarbonyl, C1-C4 alkylcarbonylamino, $-OCH_2CO_2H$, 2-(1-morpholino)ethoxy, C1-C4 alkyl (alkyl being substituted with $-N(R^{13})_2$, $-CF_3$, NO_2, or $-S(=O)R^{13a}$);

R^{13} is selected independently from: H, C1-C10 alkyl, C3-C10 cycloalkyl, C4-C12 alkylcycloalkyl, aryl, -(C1-C10 alkyl)aryl, or C3-C10 alkoxyalkyl;

R^{13a} is C1-C10 alkyl, C3-C10 cycloalkyl, C4-C12 alkylcycloalkyl, aryl, -(C1-C10 alkyl)aryl, or C3-C10 alkoxyalkyl;

when two R^{13} groups are bonded to a single N, said R^{13} groups may alternatively be taken together to form $-(CH_2)_{2-5}-$ or $-(CH_2)O(CH_2)-$;

R^{14} is OH, H, C1-C4 alkyl, or benzyl;

R^{21} and R^{23} are independently selected from:

hydrogen;

C1-C4 alkyl, optionally substituted with 1-6 halogen;

benzyl;

R^2 is H or C1-C8 alkyl;

R^{10} and R^{10a} are selected independently from one or more of the following:

phenyl, benzyl, phenethyl, phenoxy, benzyloxy, halogen, hydroxy, nitro, cyano, C1-C5 alkyl, C3-C6 cycloalkyl, C3-C6 cycloalkylmethyl, C7-C10 arylalkyl, C1-C5 alkoxy, $-CO_2R^{13}$, $-C(=O)N(R^{13})_2$, $-C(=O)NHOR^{13a}$, $-C(=O)NHN(R^{13})_2$, $=NOR^{13}$, $-B(R^{34})(R^{35})$, C3-C6 cycloalkoxy, $-OC(=O)R^{13}$, $-C(=O)R^{13}$, $-OC(=O)OR^{13a}$, $-OR^{13}$, -(C1-C4 alkyl)-OR^{13}, $-N(R^{13})_2$, $-OC(=O)N(R^{13})_2$, $-NR^{13}C(=O)R^{13}$, $-NR^{13}C(=O)OR^{13a}$, $-NR^{13}C(=O)N(R^{13})_2$, $-NR^{13}SO_2N(R^{13})_2$, $-NR^{13}SO_2R^{13a}$, $-SO_3H$, $-SO_2R^{13a}$, $-S(=O)R^{13a}$, $-SR^{13}$, $-SO_2N(R^{13})_2$, C2-C6 alkoxyalkyl, methylenedioxy, ethylenedioxy, C1-C4 haloalkyl (including $-C_vF_w$ where v = 1 to 3 and w = 1 to (2v+1)), C1-C4 haloalkoxy, C1-C4 alkylcarbonyloxy, C1-C4 alkylcarbonyl, C1-C4 alkylcarbonylamino, $-OCH_2CO_2H$, 2-(1-morpholino)ethoxy, C1-C4 alkyl (alkyl being substituted with $-N(R^{13})_2$, $-CF_3$, NO_2, or $-S(=O)R^{13a}$);

J is 3-aminopropionic acid or an L-isomer or D-isomer amino acid of structure $-N(R^3)C(R^4)(R^5)C(=O)-$, wherein:

R^3 is H or C1-C8 alkyl;

R^4 is H or C1-C3 alkyl;

R^5 is selected from:

hydrogen;

C1-C8 alkyl substituted with 0-2 R^{11};

C2-C8 alkenyl substituted with 0-2 R^{11};

C2-C8 alkynyl substituted with 0-2 R^{11};

C3-C10 cycloalkyl substituted with 0-2 R^{11};

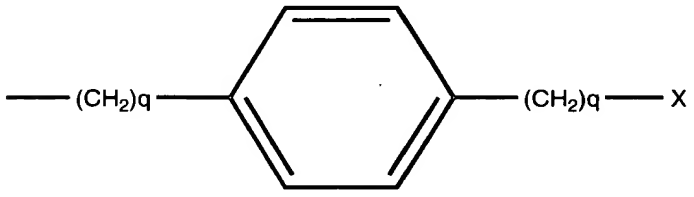
aryl substituted with 0-2 R^{12};

a 5-10-membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, or O, said heterocyclic ring being substituted with 0-2 R^{12};

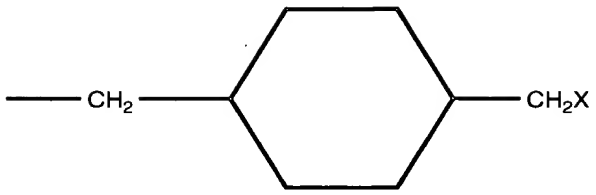
=O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{13}$, $-C(=O)R^{13}$, $-C(=O)N(R^{13})_2$, -CHO, $-CH_2OR^{13}$, $-OC(=O)R^{13}$, $-OC(=O)OR^{13a}$, $-OR^{13}$, $-OC(=O)N(R^{13})_2$, $-NR^{13}C(=O)R^{13}$, $-NR^{14}C(=O)OR^{13a}$, $-NR^{13}C(=O)N(R^{13})_2$, $-NR^{14}SO_2N(R^{13})_2$, $-NR^{14}SO_2R^{13a}$, $-SO_3H$, $-SO_2R^{13a}$, $-SR^{13}$, $-S(=O)R^{13a}$, $-SO_2N(R^{13})_2$, $-N(R^{13})_2$, $-NHC(=NH)NHR^{13}$, $-C(=NH)NHR^{13}$, $=NOR^{13}$, NO_2, $-C(=O)NHOR^{13}$, $-C(=O)NHNR^{13}R^{13a}$, $=NOR^{13}$, $-B(R^{34})(R^{35})$, $-OCH_2CO_2H$, 2-(1-morpholino)ethoxy, $-SC(=NH)NHR^{13}$, N_3, $-Si(CH_3)_3$

(C1-C5 alkyl)NHR^{16};

-(C0-C6 alkyl)X;



, where q is independently 0,1;

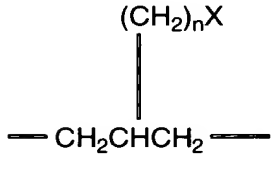


;

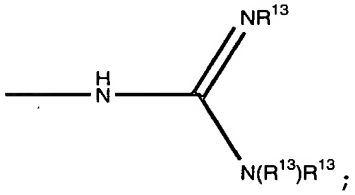
-(CH2)mS(O)p'(CH2)2X, where m = 1,2 and p' = 0-2;

~~wherein X is defined below;~~ and

R^3 and R^4 may also be taken together to form



, where n = 0,1 and X is



;

R^3 and R^5 can alternatively be taken together to form -(CH2)t- or -CH2S(O)p'C(CH3)2-, where t = 2-4 and p' = 0-2; or

R^4 and R^5 can alternatively be taken together to form -(CH2)u-, where u = 2-5;

R^{16} is selected from:

an amine protecting group;

1-2 amino acids;

1-2 amino acids substituted with an amine protecting group;

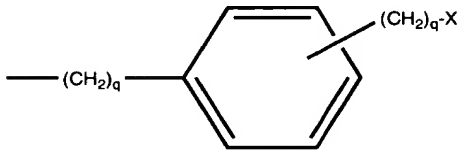
K is a D-isomer or L-isomer amino acid of structure

-N(R6)CH(R7)C(=O)-, wherein:

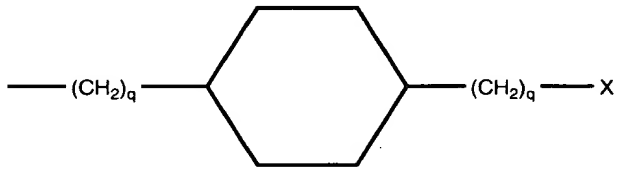
R6 is H or C1-C8 alkyl;

R7 is selected from:

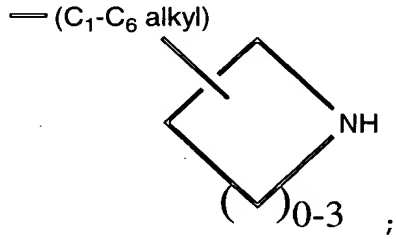
-(C1-C7 alkyl)X;



, wherein each q is independently 0-2 and substitution on the phenyl is at the 3 or 4 position;



, wherein each q is independently 0-2 and substitution on the cyclohexyl is at the 3 or 4 position;

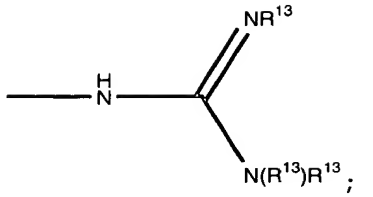


;

-(CH2)mO-(C1-C4 alkyl)-X, where m = 1 or 2;

-(CH2)mS(O)p'-(C1-C4 alkyl)-X, where m = 1 or and p' = 0-2; and

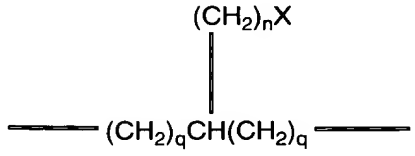
X is selected from:



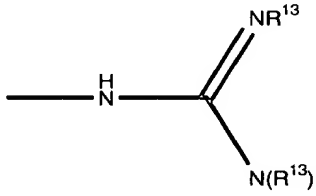
$-N(R^{13})R^{13}$; $-C(=NH)(NH_2)$; $-SC(=NH)-NH_2$;

$-NH-C(=NH)(NHCN)$; $-NH-C(=NCN)(NH_2)$; $-NH-C(=N-OR^{13})(NH_2)$;

R^6 and R^7 can alternatively be taken together to form



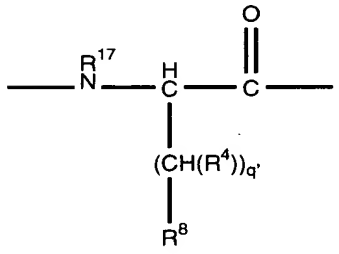
, wherein each q is independently 1 or 2 and wherein n = 0 or 1 and X is $-NH_2$

or  ;

L is $-Y(CH_2)_vC(=O)-$, wherein:

Y is NH, N(C1-C3 alkyl), O, or S; and v = 1 or 2;

M is a D-isomer or L-isomer amino acid of structure



, wherein:

q' is 0-2;

R^{17} is H, C1-C3 alkyl;

R^8 is selected from:

$-CO_2R^{13}$, $-SO_3R^{13}$, $-SO_2NHR^{14}$, $-B(R^{34})(R^{35})$, $-NHSO_2CF_3$, $-CONHNHSO_2CF_3$, $-PO(OR^{13})_2$, $-PO(OR^{13})R^{13}$, -SO2NH-heteroaryl (said heteroaryl being 5-10-membered and having 1-4 heteroatoms selected independently from N, S, or O) , -SO2NH-heteroaryl (said heteroaryl being 5-10-membered and having 1-4 heteroatoms selected independently from N, S, or O), $-SO_2NHCOR^{13}$, $-CONHSO_2R^{13a}$, $-CH_2CONHSO_2R^{13a}$, $-NHSO_2NHCOR^{13a}$, $-NHCONHSO_2R^{13a}$, $-SO_2NHCONHR^{13}$;

R^{34} and R^{35} are independently selected from:

-OH,

-F,

$-N(R^{13})_2$, or

C1-C8-alkoxy;

R^{34} and R^{35} can alternatively be taken together form:

a cyclic boron ester where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1-4 heteroatoms independently selected from N, S, or O;

a divalent cyclic boron amide where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1-4 heteroatoms independently selected from N, S, or O;

a cyclic boron amide-ester where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1-4 heteroatoms independently selected from N, S, or O.